# Metabolite concentration changes during motor activation using functional Magnetic Resonance Spectroscopy (fMRS) at 7T

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***Introduction:*** Functional MR spectroscopy (fMRS) allows to investigate the metabolic response of the brain to a physiological stimulation, by acquiring continuously MR spectra during a functional task, and provides direct insights into brain metabolism. For the studies of dynamic concentration changes using fMRS, a high time evolution is of advantage for the characterization of the very small transient changes (around 0.2µmol/g). Therefore, measurements with the highest sensitivity are desirable. Recent studies [1-3] at high field (7 Tesla) reported small metabolite concentration changes (around 0.2µmol/g) and in particular a lactate concentration increase varying between 10-23% during visual stimulation. Additionally, it is interesting to investigate metabolite changes during other stimulation. Therefore, the aim of this study was to investigate the metabolite changes during motor activation in the human brain and to compare these changes with those of visual activation.

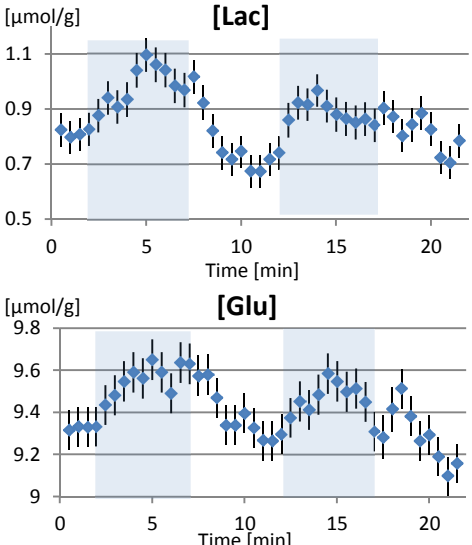
***Materials and Methods:*** Five healthy subjects (5 men aged 18 to 25 years, right-handed) gave informed consent according to the procedure approved by the local ethics committee. The experiment were performed on 7T/68cm scanner (Siemens) with the use of a 32-channel transmit/receive volume coil. A bag (10×10cm$^2$) filled with a solution of $D_2O$ and barium titanate [4] was placed between the coil and the subject's head (above the motor cortex) to increase the $B_1^+$ sensitivity in the region of interest. A preliminary fMRI experiment was performed at the beginning of the study where the subject was asked to tap each of his fingers successively against the thumb at a frequency of 3Hz (20s ON, 20s OFF, TA=2min30s). Numbers from 1 to 4 were projected on a screen at the back of the scanner and gave the finger-tapping rate. During the rest period, the subject was asked to keep his hands open and to not move his fingers. The overlap of the anatomical images (MP2RAGE [5]) and the activation map guided the placement of the VOI for the subsequent fMRS scans in an area of high motor activation (inset fig. 2). First and second order shims were adjusted using FAST(EST)MAP. For fMRS, each subject was exposed to the same motor task that the one conducted during the preliminary fMRI experiment for four alternate periods of 5min of motor activation and rest, preceded by a 2 min rest period (22min total). $^1$H MR spectra were continuously acquired using the semi adiabatic SPECIAL sequence (TR/TE=7500/12ms, BW=4000Hz, vector size=2048 pts, VOI=17*20*17mm$^3$, 88×2 scans) [6] preceded by VAPOR water and outer volume suppression [7]. The unsuppressed water signal was measured at the end of the experiment. The individual MR spectra were frequency corrected using home-written Matlab routine and summed over the 5 subjects in blocks of 10 spectra (2 scans per subject). All spectra were fitted and quantified using LCModel [8] with a basis set of simulated spectra of 20 metabolites. Only metabolites with CRLB<30% were used and metabolite concentrations are expressed in µmol/g.

***Results and Discussion:*** The dielectric pad enabled a $B_1^+$ sensitivity gain up to 30% in the region of interest based on sa2rage map comparison. Shimming resulted in typical water linewidths of 12.6±0.4Hz (mean±std, n=5). Stable and reproducible spectra were acquired during the fMRS experiment and the SNR of NAA resonance was typically 52±5 (mean±std, n=5, NT=2). The water signal was generally minimized below the height the NAA peak. The use of the semi adiabatic SPECIAL sequence at 7T and the dielectric pad yielded sufficient sensitivity to investigate the metabolite changes during functional activity in a small activated area using volume coil. Reliable quantification of the metabolite concentration allowed quantification of 13 metabolites with CRLB less than 30% (NT=10), in particular for Lac with CRLB below 20% and for Glu below 3%. Linewidth changes, induced by the BOLD effect, were observed on the time course of the creatine peak height (average increase of 1.5%) and confirmed the position of the voxel in the activated area. To study the metabolite changes, spectra were averaged between the subjects (n=5) enabling a native time resolution of 25s for the metabolite time courses (fig. 1). When comparing activation to rest for each individual subject (n=5), a relative increase of [Lac] by 28±3% (0.20±0.04 µmol/g, p<0.002) and of [Glu] by 3±1% (0.25±0.08 µmol/g, p<0.04) were found. Additionally, Glu and Lac changes were observed on the difference spectrum, after BOLD effect correction, (fig. 2) when subtracting the summed rest spectra from the summed activation spectra.

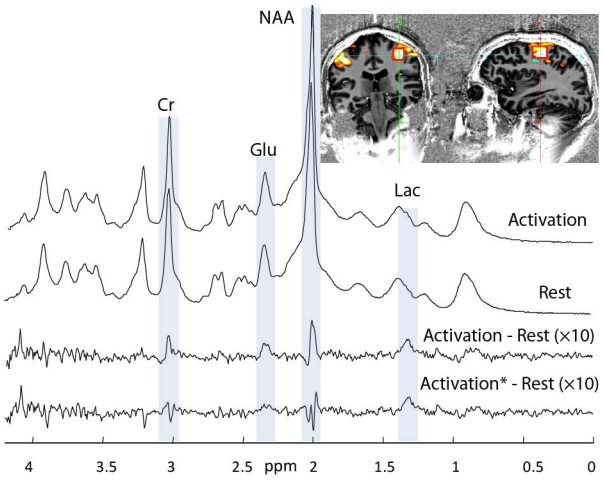
***Conclusion:*** To summarize, this study establishes that it is possible to investigate the neurochemical profile changes during motor activation. In addition, [Lac] and [Glu] increase as has been observed during visual stimulation [1-3].

We conclude that the small but significant increases in Glu and Lac are most likely a general manifestation of brain activation.

***References and Acknowledgements:*** [1] S. Mangia *et al.*, JCBFM, 27:1055-1063, 2007 [2] B. Schaller *et al.*, ISMRM 2011 Abstract # 5576 [3] Y. Lin *et al.*, JCBFM, 2012 [4] Teeuwisse *et al.* MRM, 67:1285-1293, 2012 [5] Marques JP *et al.*, Neuroimage, 2010 [6] L. Xin *et al.*, MRM, 2012 [7] I. Tkac *et al,*AMR, 29(1):139-157,2005 [8] S. Provencher, MRM, 30, 1993. Supported by CIBM of the UNIL, UNIGE, HUG, CHUV, EPFL, the Leenaards and Jeantet Foundations and SNF grant 131087.




◄***Figure 1:*** *Time courses for [Lac] and [Glu] during the functional paradigm. Each time point corresponds to 10 averaged spectra and a moving average was applied (sliding offset=4scans). Data are mean±CRLB.*




►***Figure 2:*** *Summed $^1$H spectrum acquired during stimulation **(A)** and rest **(B)** periods (n=5, NT=56) were subtracted to yield the difference spectrum **(C)**. An additional line broadening (*) of 0.35Hz was applied to the activated spectrum to correct for the BOLD effect on metabolite linewidth **(D)**. Inset: Location of the VOI (17*20*17mm$^3$, red square) in the motor cortex.*